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Review

Neurotoxic snake bites in Saudi Arabia: Current status analysis

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Abstract
Saudi Arabia has vast areas of deserts with the availability of different types of venomous snakes. Snake bites continue to be extremely dangerous injuries worldwide and occasionally need critical care. Snake bites have different systemic manifestations including hematotoxic and neurotoxic presentations. Neurotoxic bites are characterized by neurological manifestations with flaccid paralysis of the respiratory muscles which ends fatally by respiratory arrest and death. Neurotoxic snake bites were reported in Saudi Arabia with lower incidence than the hemotoxic bites. Effective handling of an envenomed patient, such as timely hospitalization, ventilator support, and antivenom administration, greatly lowers the risk of neurological complications, which lowers mortality and enhance the functional outcome of survivors.

Keywords
Neurotoxic, Snakes, Bites, Desert, Manifestations

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Introduction

Snakes are members of the reptile's family, which descended from lizards. Their sizes differ significantly, with the smallest measuring only 15 cm and the largest reaching up to 10 m. The majority of species, however, reach an adult height of 1 to 2 m [1]. Snakes have developed extra senses, most likely because their sight and hearing are insufficient. They share some of the same senses as other animals, including smell and sight. In general, temperature controls snake activity and population size. Snakes are rare in colder temperatures but common in tropical areas where they have spread to many different habitats. Certain snakes are exclusively aquatic, some are subterranean, while some spend the majority of their lives on huge forest trees [2].

Snake bites continue to be extremely dangerous injuries worldwide, occasionally need critical care [3]. There is always a chance of getting bitten by a snake, just like with malaria, dengue hemorrhagic fever, TB, and parasitic illnesses. Snake bites were included in the list of neglected tropical illnesses, along with Japanese encephalitis, cholera, and dengue hemorrhagic fever, by the World Health Organization in 2009. Compared to other neglected tropical diseases, snake bites have a far higher death rate [4]. A deadly illness, snakebite envenomation causes between 81 000 to 138 000 deaths worldwide each year [5]. The most vulnerable groups are those who work in agricultural fields, the children, and those who reside in rural areas of poverty [3, 6, 7].

A retrospective study found that youngsters in Saudi Arabia had a higher prevalence of having been bitten by a snake than the global trend [8]. Interestingly, this study showed more severe manifestations of the venomous snakebites in children when compared to adults enrolled in the study [9]. The clinical presentation of the toxic snakebites depends on the type of venomous snake, the quantity of injected venom, and a personal health status and susceptibility. Tissue necrosis, edema, and discomfort are typical local consequences. From minor nausea and vomiting to potentially fatal life-threatening neurotoxicity, cardiotoxic manifestations, renal impairment, or serious hematological consequences. These manifestations can vary widely [10, 11].

Classification of venomous snakes

Every snake that is significant to medicine has one or more sets of upper jaw fangs. These pierce the skin of their prey, allowing the venom to enter the tissues through a closed tube or groove. The Atractaspididae, Elapidae, Hydrophidae, and Viperidae families comprise venomous snakes [12]. Based on the main effects of the venom, snake venom can be categorized mainly as as hematotoxic, neurotoxic, necrotoxic, cardiotoxic, or nephrotoxic. Protein, enzymes, neurotoxins, coagulants, anticoagulants, and compounds having cytotoxic effects are some of the components that make up the venom [13].

Venoms are a complex mixture of poisonous and enzymatic proteins that, depending on the pathophysiological alterations in certain species, cause a variety of clinical symptoms [14, 15]. The Middle East is home to forty-six species of venomous snakes, five of which are found in Saudi Arabia. Three of these families are clinically significant: the Viperidae (which includes Bitis arietans, Cerastes cerastes gasparetti, Echis carinatus sochureki, Echis pyramidium, and Echis coloratus); the Elapidae (which includes Naja haje arabica and Walterinnesia aegeptia); and the Atractaspididae (which includes Atractaspis microlepidota and Atractaspis engaddensis) [13]. Elapidae bites are the most common source of neurotoxic snake bites [3].

Neurotoxic venomous snakes

Elapidae family

Elapidae members are characterized by their front permanently erected fangs in the mouth. Except for the species Emydocephalus, the majority of elapids are venomous [16]. With terrestrial species found in Asia, Australia, Africa, and the Americas and marine forms found in the Pacific and Indian Oceans, elapids are indigenous to tropical and subtropical locations worldwide. The family's members range widely in size, from 0.18 to 5.85 m in white-lipped snake and king cobra, respectively [1]. Through their hollow fangs, the majority of species channel their neurotoxic venom; others may also contain additional harmful ingredients in different amounts. To inject venom from glands toward the back of the upper jaw, all elapids possess a pair of proteroglyphous fangs [17]. The two primary Elapidae family members in Saudi Arabia are Walterinnesia aegeptia and Naja haje arabica [13].

Neurotoxic Snake venom

The primary neurotoxic effect of Elapidae venom is used to immobilize prey and for defense. Three-finger toxins (3FTx) and PLA2 comprise the majority of the toxins. Other harmful elements found in certain species include cytotoxins and cardiotoxins, which harm cells and induce cardiac problems, respectively. Hemostases, which cause blood to clot or harden, are also present in cobra venom [17].

The capacity of large species, such as cobras and mambas, to inject copious amounts of venom during a single envenomation and/or to strike at a high point close to the victim's brain, which is susceptible to neurotoxicity, makes them dangerous [18]. Spitting cobras produce cytotoxic venom as opposed to neurotoxic venom. It harms local cells, particularly those in the eyes, which the snakes specifically target. When venom gets in the eye, it can hurt so much that it can induce blindness. If there is no wound that would allow the poisons to enter the bloodstream, it is not fatal when applied topically [19].

Clinical Features of neurotoxic snakebite

The majority of the bites from neurotoxic snakes only had minor local characteristics, such as the fang marks. Rare symptoms include bleeding, edema, and pain. In general, symptoms including flushing, dyspnea, palpitations, lightheadedness, chest tightness, perspiration, and acroparaesthesiae are frequent. These result from overactive sympathetic nervous system and anxiousness [20]. In addition, vomiting, heavy eyelids, blurred vision, hypersalivation, congested conjunctivae, and "gooseflesh" are among the initial symptoms of elapid bites. cramping stomach ache and diarrhea after krait bites [21].

Venoms from elapids are very neurotoxic. Elapid bites cause ptosis and external ophthalmoplegia, which can emerge as soon as 15 minutes after the bite and are the initial signs of paralysis. On occasion, the onset could be postponed for up to ten hours. Subsequently, paralysis occurs in the muscles of the neck, deglutition muscles, tongue, jaws, palate, and voice cords. Respiratory failure is brought on by blockage of the airways or

paralysis of the diaphragm and intercostal muscles. The effects of neurotoxic substances can be entirely reversed, either immediately by using antivenom or anticholinesterases, or they can go away on their own in one to seven days [22-24]. It is noteworthy that these neurotoxins do not change consciousness or pass through the blood-brain barrier [24]. Furthermore, bradycardia, tachycardia, hypotension, and arrhythmias are examples of direct cardiac injury that can result from elapid venom. Numerous factors can lead to shock, which can happen for various reasons. Among them are cardiac depression and fear [22].

Limited information was found when the literature on neurogenic snakebites in Saudi Arabia was reviewed. According to one study, a single case of bulbar palsy appeared six hours after the bite and became better one and a half hours after receiving AV infusion. According to snake description, the cobra snake Naja haje arabicus was suggested as the involved snake [24]. Two more case reports, one describing a vegetative state and intracranial hemorrhage [25] and the other imitating brain death with respiratory arrest [26] following neurotoxic snakebites. Alfaifi et al. [7] study, which examined thirteen individuals with neurologic features—defined as altered mental status, respiratory impairment, or ophthalmoplegia—provided the most extensive data regarding neurotoxic snake bites in Saudi Arabia. Three of them showed signs of moderate ptosis, diplopia, or dyspnea. The remaining ten had moderate-to-severe presentations, which included respiratory paralysis, cardiopulmonary arrest, and bewilderment. The most typical neurogenic symptom was altered mental status.

Interestingly, Alfaifi et al.'s article [7] reports that a patient who had Echis coloratus envenomation also had proximal weakness and ophthalmoplegia, indicating the possibility of neurogenic effects from snakes other than elapids in Saudi Arabia including other viperid species. This discovery highlights the necessity for additional investigation into the venom profiles of local snakes and their distinct neurotoxic constituents.

Management of neurotoxic snake bite

First aid

As soon as possible, the patient needs to be reassured and taken to the closest hospital. A splint or sling should be used to immobilize the biting portion. Compression bandages and tourniquets should only be used with caution in cases of severe sea snake or elapid bites if getting to a medical facility would likely take longer than two to three hours but less than an hour [27]. Here, tourniquets and compression assist in postponing the venom's absorption and the subsequent development of respiratory muscle paralysis. The tourniquet should be just tight enough to obstruct venous and lymphatic flow, but not arterial flow. The rule of thumb is that it should be sufficiently slack to allow a finger to pass under it. Every fifteen minutes, the tourniquet should be removed for thirty seconds to allow the venom to slowly leak into the bloodstream and neutralize it. After administering the first dosage of antivenom, the tourniquet should only be removed [28, 29]. Use sterile cotton gauze to carefully clean the bite wound. Only utilize the intravenous method for medicines if there is incoagulable blood or seeping from puncture wounds [30].

Evaluation in the hospital

If any of the following occur at the bite site and its extension—such as swelling, blistering, or necrosis—the bite is said to have been poisonous. Shock or hypotension, hemorrhage, myoglobinuria, bradycardia, tachycardia, neuroparalytic symptoms, and laboratory evidence of coagulation malfunction are all suggestive manifestations of toxic snake bites [31].

Antivenom therapy

Whether or not to inject antivenom is the most crucial decision in managing a case of snakebite. Research indicates that the advantages of this treatment greatly exceed the possibility of side effects in individuals with severe envenomation [32]. Neurotoxicity manifestation, hypotension, shock, irregular ECG, any other symptom of cardiovascular malfunction, impaired awareness, or generalized rhabdomyolysis are common indications for the delivery of antivenom in situations of neurotoxic bites. As long as systemic indications of envenoming continue, it is virtually never too late to administer anti-venom [31].

The National Antivenom and Vaccine Production Centre, the manufacturer in Saudi Arabia, suggests administering 4-6 vials of polyvalent snake antivenom as an initial dosage, with the option to re-administer it dependent on clinical response [7]. According to reports from Saudi Arabia, neurologic envenoming cases required an average antivenom dose of 22 vials. Re-administration was necessary in up to 39% of treated cases, indicating the possibility of ongoing antivenom therapy being necessary to get the best possible clinical response [7]. Up to 9% of our patients experienced minor and temporary allergic reactions to antivenom in the Saudi investigations [24-26]. The comparatively low incidence of severe allergic reactions supports the continued use of antivenom as the main treatment for snakebite.

Anticholinesterase medication

It is commonly acknowledged that anticholinergics can reverse reversal, which is the inhibition of cholinesterase at the NMJ leading to elevated acetylcholine concentrations, after neurotoxic snake bites. Increased acetylcholine displaces nicotinic receptor competitive antagonists, restoring function of the NMJ, particularly in cases where ophthalmoplegia is present. [25, 33] Alfaifi et al. [25] from Saudi Arabia reported on the application of antivenene and anticholinergic combo therapy for imitating cobra bite-induced brain death. Additionally, Alfaifi et al. [7] reported in their study that three patients arrived at the emergency room with respiratory arrest mimicking brain death, ventricular fibrillation cardiac arrest, and anticholinesterase medication for suspected neurogenic envenomation, while the third case was represented with asystole cardiac arrest. Neostigmine, pyridostigmine, physostigmine were reported to be used for these cases.

Discussion

Conclusion

Saudi Arabia's diverse snake species pose a serious threat to public health because they can cause a wide range of clinical manifestations, from minor local envenomation to potentially fatal consequences like coagulation disorders, compartment syndrome, respiratory faliure, and even cardiorespiratory arrest. Our research highlights the significance of raising public

awareness about lethal snakebites and the need to administer first aid correctly, avoiding the use of ineffective traditional beliefs that could worsen conditions or even prolong death.

It is important to improve the knowledge of the physicians and emergency personnel about the venomous snakes in Saudi Arabia and their pattern of clinical presentations, which may be mild and may extend to a state mimicking brain death, which must be evaluated and investigated to save it from the diagnosis errors the brain death. In addition, they should be aware of the atypical manifestations of certain snakes' bites and they should know that the venom contains different types of toxins, which may be manifested in different proportions. This emphasizes the significance of early diagnosis and treatment, especially for neurotoxic envenomation, and the necessity for physicians in the area to be knowledgeable about the range of snakebite manifestations.

Additionally, it is critical to address snakebite cases comprehensively and holistically, with the right dosage based on the severity and particular clinical circumstances of each case. Antivenin therapy continues to be based on supportive care and antivenin. Given the high prevalence of coagulopathy and other significant effects in Saudi Arabia, it is imperative to regularly monitor patients, promptly identify issues, perform a thorough neurological evaluation in all suspected cases of snakebites, and take prompt treatment to improve the patient's prognosis.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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